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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/069,314	02/13/2002	Shigenori Ohkawa	2629 USOP	8097

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EXAMINER

COLEMAN, BRENDA LIBBY

ART UNIT

PAPER NUMBER

1624

DATE MAILED: 12/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/069,314

Applicant(s)

OHKAWA ET AL.

Examiner

Brenda Coleman

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 October 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4, 6-20 and 26-29 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 10, 11, 18-20 and 26-29 is/are rejected.
- 7) ☒ Claim(s) 6-9 and 12-17 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 10/04.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Claims 1-4, 6-20 and 26-29 are pending in the application.

This action is in response to applicants' amendment filed October 8, 2004.

Claims 5, 21-25 and 30-33 were canceled and claims 1-4, 10-13, 20 and 26-29 were amended.

Response to Amendment

Applicant's amendments filed October 8, 2004 have been fully considered with the following effect:

1. The applicants' amendments and arguments are sufficient to overcome the improper Markush rejection labeled paragraph 2 of the last office action, which is hereby **withdrawn**.
2. With regards to the 35 U.S.C. § 112, first paragraph rejection of claims 18 and 20-33 of the last office action, applicants' state that "the specification provides enough detail for one skilled in the art of synthesis to understand the invention". However, the definition of prodrug in the specification is such that prodrug refers to a compound which is converted to Compound (I) under the physiological condition or with a reaction due to an enzyme, an gastric acid, etc. in the living body, that is a compound which is converted to Compound (I) with enzymatic oxidation, reduction, hydrolysis, etc. according to an enzyme, a compound which is converted to Compound (I) with hydrolysis by gastric acid, etc.

The term pro-drug is of indeterminate scope in that they vary widely from drug to drug. It is not known which moiety of formula (I) would form the basis for the pro-drug.

Every ester, amide and carbamate in theory is biohydrolyzable, i.e. is capable in some degree of hydrolyses. Not to mention the many in vivo environments that this occurs in. It is the Wands factors, which are used to evaluate the enablement question. In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988); Ex parte Forman, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

The nature of the invention in the instant invention, has claims which embrace substituted tricyclic compounds. The instant compounds of formula (I) wherein the prodrugs are not described in the disclosure in such a way the one of ordinary skill in the art would not know how to prepare the various compounds suggested by claims 18 and 20-33. In view of the lack of direction provided in the specification regarding starting materials, the lack of working examples, and the general unpredictability of chemical reactions, it would take an undue amount of experimentation for one skilled in the art to make the claimed compounds and therefore practice the invention.

Claims 18, 20 and 26-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record and stated above.

3. With regards to the 35 U.S.C. § 112, first paragraph rejection of claims 23-33 of the last office action, applicants' state that claims 23-25 and 30-33 have been cancelled,

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rendering the aspect of the rejection related to these claims moot and that neither claim 26 or claim 27 as amended contains the term "prevention". However, the 35 U.S.C. § 112, first paragraph rejection of claims 26-29 is to the enablement of the compounds for treating cerebrovascular impairment, cranial trauma, neurodegenerative disease (claim 26), dysuria or urinary incontinence (claim 27), preventing or treating restenosis (claim 28) and inhibiting lipid peroxidation (claim 29). The applicants provided three journal articles, of which only one is prior to the filing date, i.e. Delanty et al. This article indicates that trials of various antioxidants have a negative effect on several diseases and/or disorders as shown in Table 1 of which the applicants are urging treatment. While antioxidants have shown been shown to have a positive effect in Alzheimer's Disease, this does not provide enablement for the treatment and/or prevention of the diseases and disorders claimed herein.

Claims 26-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record and stated above.

4. The applicants' amendments and arguments are sufficient to overcome the 35 U.S.C. § 112, second paragraph rejections labeled paragraph 6 of the last office action, which are hereby **withdrawn**.

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5. The applicants' amendments and arguments are sufficient to overcome the 35 U.S.C. § 101, rejection labeled paragraph 7 of the last office action, which is hereby **withdrawn**.

6. With regards to the 35 U.S.C. § 102, anticipation rejection of claims 1 and 19 of the last office action, applicants' state that "ring A of the compounds of the present invention as set forth in independent claim 1 as amended is made of carbon and nitrogen atoms". However, the claim language of independent claim 1 is such that ring A is a non-aromatic 5-membered nitrogen-containing heterocyclic ring which contains at least one nitrogen atom in addition to carbon atoms. Contains is open ended and thus can include more than just pyrrolidine rings.

Claims 1-4, 10, 11, 19 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Bhalerao et al., Arzneimittel-Forschung, for reasons of record and stated above.

7. The applicants' amendments and arguments are sufficient to overcome the 35 U.S.C. § 103, obviousness rejection labeled paragraph 9 of the last office action, which is hereby **withdrawn**.

8. The applicants' amendments and arguments are sufficient to overcome the obviousness-type double patenting rejection labeled paragraph 10 of the last office action, which is hereby **withdrawn**.

9. The applicants' amendments and arguments are sufficient to overcome the objection labeled paragraph 10 of the last office action, which is hereby **withdrawn**.

In view of the amendment dated October 8, 2004, the following new grounds of rejection apply:

Specification

10. The disclosure is objected to because of the following informalities: the specification includes a limitation of 2.0 to about 1.0 mole with respect to the base used, in the second paragraph starting on page 76 which is further limited, i.e. preferably about 2.0 to about 5.0 which is broader.

Appropriate correction is required.

Claim Objections

11. Claims 6-9 and 12-17 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Coleman whose telephone number is 571-272-0665. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink that reads "Brenda Coleman". The signature is fluid and cursive, with the first and last names being clearly legible.

Brenda Coleman
Primary Examiner Art Unit 1624
December 23, 2004